blepharophimosis, ptosis, and epicanthus inversus syndrome

Blepharophimosis, ptosis, and epicanthus inversus syndrome (BPES) is a condition that mainly affects development of the eyelids. People with this condition have a narrowing of the eye opening (blepharophimosis), droopy eyelids (ptosis), and an upward fold of the skin of the lower eyelid near the inner corner of the eye (epicanthus inversus). In addition, there is an increased distance between the inner corners of the eyes (telecanthus). Because of these eyelid abnormalities, the eyelids cannot open fully, and vision may be limited.

Other structures in the eyes and face may be mildly affected by BPES. Affected individuals are at an increased risk of developing vision problems such as nearsightedness (myopia) or farsightedness (hyperopia) beginning in childhood. They may also have eyes that do not point in the same direction (strabismus) or "lazy eye" (amblyopia) affecting one or both eyes. People with BPES may also have distinctive facial features including a broad nasal bridge, low-set ears, or a shortened distance between the nose and upper lip (a short philtrum).

There are two types of BPES, which are distinguished by their signs and symptoms. Both types I and II include the eyelid malformations and other facial features. Type I is also associated with an early loss of ovarian function (primary ovarian insufficiency) in women, which causes their menstrual periods to become less frequent and eventually stop before age 40. Primary ovarian insufficiency can lead to difficulty conceiving a child (subfertility) or a complete inability to conceive (infertility).

Frequency

The prevalence of BPES is unknown.

Genetic Changes

Mutations in the *FOXL2* gene cause BPES types I and II. The *FOXL2* gene provides instructions for making a protein that is active in the eyelids and ovaries. The FOXL2 protein is likely involved in the development of muscles in the eyelids. Before birth and in adulthood, the protein regulates the growth and development of certain ovarian cells and the breakdown of specific molecules.

It is difficult to predict the type of BPES that will result from the many *FOXL2* gene mutations. However, mutations that result in a partial loss of FOXL2 protein function generally cause BPES type II. These mutations probably impair regulation of normal development of muscles in the eyelids, resulting in malformed eyelids that cannot open

fully. Mutations that lead to a complete loss of FOXL2 protein function often cause BPES type I. These mutations impair the regulation of eyelid development as well as various activities in the ovaries, resulting in eyelid malformation and abnormally accelerated maturation of certain ovarian cells and the premature death of egg cells.

Inheritance Pattern

This condition is typically inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

In some cases, an affected person inherits the mutation from one affected parent. Other cases result from new mutations in the gene and occur in people with no history of the disorder in their family.

Other Names for This Condition

- blepharophimosis syndrome
- blepharophimosis, ptosis, and epicanthus inversus
- BPES

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Blepharophimosis, ptosis, and epicanthus inversus https://www.ncbi.nlm.nih.gov/gtr/conditions/C0220663/

Other Diagnosis and Management Resources

- GeneReview: Blepharophimosis, Ptosis, and Epicanthus Inversus https://www.ncbi.nlm.nih.gov/books/NBK1441
- MedlinePlus Encyclopedia: Ptosis https://medlineplus.gov/ency/article/001018.htm

General Information from MedlinePlus

- Diagnostic Tests https://medlineplus.gov/diagnostictests.html
- Drug Therapy https://medlineplus.gov/drugtherapy.html
- Genetic Counseling https://medlineplus.gov/geneticcounseling.html

- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Epicanthal folds
  https://medlineplus.gov/ency/article/003030.htm
- Encyclopedia: Ptosis
  https://medlineplus.gov/ency/article/001018.htm
- Health Topic: Amblyopia
  https://medlineplus.gov/amblyopia.html
- Health Topic: Eyelid Disorders
  https://medlineplus.gov/eyeliddisorders.html
- Health Topic: Premature Ovarian Failure
  https://medlineplus.gov/prematureovarianfailure.html

Genetic and Rare Diseases Information Center

- Blepharophimosis, ptosis, and epicanthus inversus syndrome type 1
  https://rarediseases.info.nih.gov/diseases/23/blepharophimosis-ptosis-and-epicanthus-inversus-syndrome-type-1
- Blepharophimosis, ptosis, and epicanthus inversus syndrome type 2
  https://rarediseases.info.nih.gov/diseases/10213/blepharophimosis-ptosis-and-epicanthus-inversus-syndrome-type-2

Additional NIH Resources

- National Institute of Child Health and Human Development: Primary Ovarian Insufficiency
  https://www.nichd.nih.gov/health/topics/POI/Pages/default.aspx

Educational Resources

- Disease InfoSearch: Blepharophimosis Syndrome Type 1
  http://www.diseaseinfosearch.org/Blepharophimosis+Syndrome+Type+1/870
- Disease InfoSearch: Blepharophimosis Syndrome Type 2
  http://www.diseaseinfosearch.org/Blepharophimosis+Syndrome+Type+2/871
- Orphanet: Blepharophimosis-epicanthus inversus-ptosis syndrome
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=126

- The University of Arizona: Hereditary Ocular Disease
  http://disorders.eyes.arizona.edu/handouts/bpes-syndrome
- University of Iowa Health Care
  http://webeye.ophth.uiowa.edu/eyeforum/cases-i/case114/BPES.html
- Washington Univeristy, St. Louis: Neuromuscular Disease Center
  http://neuromuscular.wustl.edu/syncm.html#blepharophimosis

Patient Support and Advocacy Resources

- CLIMB: Children Living with Inherited Metabolic Diseases
  http://www.climb.org.uk/
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/blepharophimosis-ptosis-epicanthus-inversus-syndrome/
- RESOLVE: The National Infertility Association: Premature Ovarian Failure
  http://www.resolve.org/about-infertility/medical-conditions/premature-ovarian-failure-1.html
- University of Kansas Medical Center Resource List
  http://www.kumc.edu/gec/support/blepharo.html

GeneReviews

- Blepharophimosis, Ptosis, and Epicanthus Inversus
  https://www.ncbi.nlm.nih.gov/books/NBK1441

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28blepharophimosis+ptosis+epicanthus+inversus%5BTIAB%5D%29+OR+%28blepharophimosis+syndrome%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- BLEPHAROPHIMOSIS, PTOSIS, AND EPICANTHUS INVERSUS
  http://omim.org/entry/110100

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